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**Direct reprogramming of fibroblasts into cardiomyocytes for cardiac regenerative medicine.**

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**Public Summary:**

Structural cells in the heart called cardiac fibroblasts play critical roles in maintaining normal heart function during a heart attack. Adult heart muscle cells have little to no regenerative capacity; damaged cells in the heart after a heart attack are replaced by cardiac fibroblasts, ultimately leading to scarring and reduced cardiac function. Our lab and others have shown that heart function may someday be restored through the process of direct reprogramming. This process takes adult cardiac fibroblasts and transforms them into cardiac muscle-like cells. Direct cardiac reprogramming also provides a new research model to investigate which genes control the molecular network that guides cardiac cell fate. Here we review the approaches of in vitro and in vivo reprogrammed cells from different laboratories, and outline the future directions needed to translate this new approach into a practical therapy for damaged hearts.

**Scientific Abstract:**

Cardiac fibroblasts play critical roles in maintaining normal cardiac function and in cardiac remodeling during pathological conditions such as myocardial infarction (MI). Adult cardiomyocytes (CMs) have little to no regenerative capacity; damaged CMs in the heart after MI are replaced by cardiac fibroblasts that become activated and transform into myofibroblasts, which preserves the structural integrity. Unfortunately, this process typically causes fibrosis and reduces cardiac function. Directly reprogramming adult cardiac fibroblasts into induced CM-like cells (iCMs) holds great promise for restoring heart function. Direct cardiac reprogramming also provides a new research model to investigate which transcription factors and microRNAs control the molecular network that guides cardiac cell fate. We review the approaches and characterization of in vitro and in vivo reprogrammed iCMs from different laboratories, and outline the future directions needed to translate this new approach into a practical therapy for damaged hearts.

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